REMARKS

Applicants thank the Examiner and the supervisory Examiner for the personal interview of October 22, 2009.

After entry of this amendment, claims 1, 3-18 and 20-25 are pending, of which claims 4-6, 16-18, 20, and 21 are withdrawn. The claims have been amended without prejudice or disclaimer and find support *inter alia* in the original claims. Claim 1 finds further support in the specification, for example, at page 25, lines 38-48. Claim 3 finds further support in the specification, for example, at page 5, lines 9-11, and page 22, lines 18-22. Claims 9, 12, 15, 24 and 25 have been amended without prejudice or disclaimer to correct the antecedent basis. No new matter has been added.

In the event that claim 1 is found allowable, then rejoinder of the non-elected subject matter that depends from or otherwise includes all the limitations of the allowed claim is respectfully requested. MPEP § 821.04(b).

Claim Rejections – 35 U.S.C. § 112

Claims 1, 7-15 and 22-25 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement and allegedly lacking an enabling disclosure. Applicants strongly disagree and traverse the rejections for the reasons already of record and for the following additional reasons.

Written Description Rejection

The Examiner rejects claims 1, 7-15 and 22-25 under 35 U.S.C. § 112, first paragraph, for alleged lack of an adequate written description support.

The Examiner contends that 284-base-pair long fragments of a promoter sequence cannot predictably be assumed to have the same promoter activity. By interpreting a "fragment" as encompassing di-nucleotide, the Examiner further argues that di-nucleotide fragments of a promoter sequence do not have promoter activity, citing to Maiti *et al.* and Doelling *et al.* for support. Moreover, the Examiner argues that the prediction of tissue specificity of a promoter sequence, mutation of promoter sequences, as well as identification of the functional parts of promoters is unpredictable, citing to Bustos *et al.*, Donald *et al.*, Eyal *et al.*, Chen *et al.*, Benfey

et al., and Kim *et al.* for support. Additionally, the Examiner also contends that the specification does not describe any particular *cis* elements that are required for the tissue specificity of SEQ ID NO: 1. Applicants strongly disagree.

"The burden of showing that the claimed invention is not described in the application rests on the PTO in the first instance." *In re Edwards,* 568 F.2d 1349, 1354 (CCPA 1978); Ex *parte Heck,* Appeal 2008-2875 (BPAI 2008). A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. See, e.g., *In re Marzocchi,* 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971).

Moreover, as set forth in *Vas-Cath Inc. v. Mahurkar,* 19 USPQ2d 1111, 1116 (Fed. Cir. 1991), the test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to one skilled in the art that the inventor had possession of the claimed subject matter at the time of filing. *See also, Capon v. Eshhar,* 418 F.3d 1349, 1357, 76 USPQ2d 1078, 1084 (Fed. Cir. 2005) (the "written description" requirement under 35 U.S.C. § 112, first paragraph, serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed); *see also* MPEP § 2163. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of structural chemical formulas to show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. *See* MPEP § 2163 (citation omitted).

It is noted initially that the Examiner's position is based in part, on the alleged lack of promoter activity of di-nucleotide fragments. Regardless whether a "fragment" of a nucleic acid sequence can be di-nucleotide as characterized by the Examiner, Applicants wish to draw the Examiner's attention to the further limitation recited in the claims directing to the embodiments encompassing "fragments." As recited in the claims, fragments of SEQ ID NO: 1 must also have the promoter activity of SEQ ID NO: 1, i.e. directing expression of a nucleic acid sequence of interest at least in leaf tissue but not in seed. Thus, even if di-nucleotide can be a "fragment" as alleged by the Examiner, if such di-nucleotide does not have promoter activity, specifically the

promoter activity of SEQ ID NO: 1, such di-nucleotide would not be encompassed by the claims. Accordingly, Applicants believe that the Examiner's argument on this point does not support the written description rejection.

The Examiner's position is also based in part, on the alleged lack of description regarding particular *cis* elements that are required for the tissue specificity of SEQ ID NO: 1. As mentioned above, the test for determining compliance with the written description requirement is whether the specification as originally filed reasonably conveys to a skilled artisan that the inventor had possession of the claimed subject matter at the time of filing. Describing distinguishing identifying characteristics such as *cis* elements that are required for the tissue specificity of a promoter sequence is only one of the various ways to show possession of the claimed invention. So long as possession may be shown by other acceptable means, such as by describing an actual reduction to practice or by showing that the invention was "ready for patenting," then the written description requirement is met and the Patent Office should demand no more.

Here, the present application describes an actual reduction to practice by providing an expression construct comprising the promoter sequence of SEQ ID NO: 1 for the expression of a nucleic acid sequence of interest at least in leaf tissue but not in seed, for instance, in Examples 3-8. Thus, possession of the claimed subject matter is shown, and the rejection should be withdrawn for this reason alone.

Additionally, the present application further shows that the invention was "read for patenting" by disclosing structural chemical formulas to show that the invention was complete. Here, the specification explicitly teaches the structure of promoter sequences by providing the nucleic acid sequence of SEQ ID NO: 1. The specification further exemplifies functional equivalent fragments of SEQ ID NO: 1 by providing the fragments comprising a sequence from about base pair 300 to about base pair 583 of SEQ ID NO: 1, or a sequence from about base pair 300 to about base pair 828 of SEQ ID NO: 1. A skilled artisan would thus know the structure of promoter sequences, *i.e.* fragments of SEQ ID NO: 1 or those having at least 98% identity to SEQ ID NO: 1. While the claims relate to fragments of SEQ ID NO: 1 and to sequences having at least 98% identity with SEQ ID NO: 1, "these groups define a subset of sequences fully described by SEQ ID NO: 1." *See Ex parte Heck,* Appeal 2008-2875 (BPAI 2008). As found in

Ex parte Heck, the structure of the claimed fragments and sequences having at least 98% identity to SEQ ID NO: 1 was provided and thus described. As such, one of ordinary skill in the art would conclude that Applicants were in possession of the claimed genus at the time the application was filed. Accordingly, possession of the claimed subject matter is further proven, and the rejection should be withdrawn for this additional reason.

The Examiner also asserts that the specification does not describe any expression patterns for transformed maize past the T_0 stage or for any fragment of SEQ ID NO: 1, including the fragment of bases 300 to 583 of SEQ ID NO: 1 or one that is as small as dinucleotide. Regardless of whether the activity has been shown at the plantlet stage or in further generations, the specification has nonetheless demonstrated in working examples the claimed promoter activity in at least three different plant species. With this regard, Applicants note that there has never been a requirement that every species encompassed by a claim must be disclosed or exemplified in a working example. See *In re Angstadt*, 537 F.2d 498 (CCPA 1976).

For at least the above reasons and for the reasons already of record, reconsideration and withdrawal of the rejection is respectfully requested.

Enablement Rejection

The Examiner further rejects claims 1, 3, 7-15 and 22-25 under 35 U.S.C. § 112, first paragraph, for alleged lack of an enabling disclosure.

The Examiner alleges that the specification is enabling for a promoter comprising a fragment of SEQ ID NO: 1 with promoter activity in tissues of Arabidopsis or canola, but not enabling for equivalents or variants of SEQ ID NO: 1 or promoter activity in leaves but not seeds of any other plants. The Examiner further argues that the art is so unpredictable as to render any homologs or variants that retain promoter activity of SEQ ID NO: 1 non-enabled, citing various references. Additionally, the Examiner notes that the promoter causes different expression patterns in different plants. Applicants strongly disagree.

It is noted initially that the disclosure provided in the specification is presumptively enabling. The manner of making and using the claimed invention must be taken as in compliance with the first paragraph of 35 U.S.C. §112, unless there is objective evidence or scientifically based reasoning inconsistent with the specification. *See In re Marzocchii and*

Horton, 169 U.S.P.Q. 367 (C.C.P.A. 1971). "It is the Patent Office's burden to present evidence that there is some reason to dispute the enablement provided in the specification. Unsupported speculation or conjecture on that the invention 'might not work' will not support a rejection based on 35 U.S.C. §112, first paragraph." *Id.* Simply pointing to the absence of a working example provides neither objective evidence nor reasoning in support of the rejection, and accordingly, a *prima facie* case of non-enablement on this ground has not been made out. Moreover, there has never been a requirement that every species encompassed by a claim must be disclosed or exemplified in a working example. *In re Angstadt*, 537 F.2d 498 (CCPA 1976). Additionally, even though practicing the full scope of the claims might have required some amount of experimentation, if the experimental techniques are well-known in the art, the experimentation is routine and not undue. See *Ex parte Kubin*, 83 USPQ2d 1410 (B.P.A.I. 2007), *aff'd on other ground*, 90 USPQ 2d 1417 (Fed. Cir. 2009).

Here, the specification provides working examples using the promoter sequence of SEQ ID NO: 1 to demonstrate the tissue specificity in at least three plant species, Arabidopsis, canola, and maize. The working examples provided in the specification describe, in detail, how to clone a ptxA promoter (Example 3), how to prepare an expression construct containing a ptxA promoter (Example 4), how to transform such an expression construct into a plant (Example 5), how to detect the tissue-specific expression (Example 6), and how to analyze the ptxA promoter expression pattern in different plant species (Examples 7, 10-11, 16 and 17). The methodologies described in the specification are applicable not only to the full-length of SEQ ID NO: 1 as exemplified, but also any other sequences derived from SEQ ID NO: 1 such as a fragment of SEQ ID NO: 1 or a nucleic acid sequence having at least 98% identity to SEQ ID NO: 1. Thus, although some testing and screening would be required to identify nucleic acid sequences derived from SEQ ID NO: 1 having the promoter activity of SEQ ID NO: 1, such testing and screening would not be extensive and is routine in nature, and thus, not undue.

The above analysis is also consistent with the Board's finding in *Ex parte Heck*, where the Board found that the experimentation required for promoter analysis is routine in nature, as demonstrated by two of the references cited by the Examiner in the instant Office Action, i.e. Donald and Kim. *Ex parte Heck*, Appeal 2008-2875. Moreover, as found by the Board in *Ex parte Heck*, "it is well within the level of ordinary skill in the art to prepare nucleic acid

sequences that are 98% identical to SEQ ID NO: 1." *Id.* Similarly, Applicants respectfully submit that it is also well within the level of a skilled artisan to prepare nucleic acid sequences that are fragments of a known nucleic acid sequence such as SEQ ID NO: 1 in the present case.

The Examiner further cites to the thesis by David Phillip Bown (hereinafter "Bown") for allegedly teaching that the tissue specificity is unpredictable and is species-dependent, and concludes that claims to particular tissue specificity are enabled only for the plants in which a tissue-specificity has been determined. Applicants strongly disagree with the Examiner's characterization of Bown and conclusions for the reasons already of record.

In view of the detailed description, guidance, working examples, knowledge of the art, and high level of skill, the specification enables the full scope of the claims as amended without undue experimentation. On these facts, an analysis under *In re Wands* supports enablement. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (routine screening of hybridomas was not "undue experimentation"; the involved experimentation can be considerable, so long as "routine").

For at least the above reasons and for the reasons already of record, Applicants respectfully submit that the art and the specification provide ample guidance and predictability for the present claims and the Examiner has not presented the evidence necessary to dispute the enablement provided in the instant specification. Because the Patent Office has not met its burden, reconsideration and withdrawal of the enablement rejections is respectfully requested.

Claim Rejections – 35 U.S.C. § 103(a)

Claims 1, 3, 8-15 and 22-25 are rejected under 35 U.S.C. § 103(a) as being obvious over Henkes *et al.* (hereinafter "Henkes") in view of Bown (X67427, hereinafter "Bown-2"). Applicants strongly disagree and traverse the rejection for the reasons already of record and for the following additional reasons.

The examiner bears the initial burden of establishing *prima facie* obviousness. See *In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). To support a *prima facie* conclusion of obviousness, the prior art must disclose or suggest all the limitations of the claimed invention. See *In re Lowry*, 32 F.3d 1579, 1582 (Fed. Cir. 1994).

Henkes discloses transgenic plants transformed with a stress-related protein coding nucleic acid, wherein the expression of the nucleic acid sequence in the plant results in increased

tolerance to environmental stress as compared to a wild type plant. Henkes further provides a list of promoters that can be used to express the disclosed stress-related protein coding nucleic acid. Amongst is the ptxA promoter, which is identified as being a stress-inducible promoter. See Henkes at page 16, paragraph [0107]. Henkes does not teach or suggest any other expression pattern of the ptxA promoter, let alone the tissue specificity as identified by the inventors of the present application.

Bown-2 discloses *Pisum sativum* ptxA gene with a total length of 3234 base pairs, which includes 943 base pairs upstream of the coding region. This 943-bp region upstream of the ptxA coding sequence presumably comprises the promoter of the ptxA gene. However, Bown-2 does not teach or suggest the expression profile of the ptxA gene. Nor does Bown-2 teach or suggest the tissue specificity of the promoter of the ptxA gene.

It follows that, neither Henkes nor Bown-2, alone or in combination, teach or suggest the tissue specificity of the ptxA promoter in directing expression at least in leaves but not in seeds. Because Henkes and Bown-2, alone or in combination, do not teach all of the claim limitations, a *prima facie* case of obviousness has not been established. Accordingly, the rejection should be withdrawn for this reason alone.

Nevertheless, the Examiner alleges the tissue specificity such as expression in leaves but not seeds is merely an intrinsic property which would naturally flow from utilizing the ptxA promoter of Bown-2 as suggested in Henkes even for a different purpose. Applicants strongly disagree with the Examiner's application of inherency in the context of this obviousness rejection.

It is well established that inherency of missing features/limitations is limited to the context of anticipation under 35 U.S.C. § 102. In other words, obviousness under 35 U.S.C. § 103(a) cannot be established through inherency. Moreover, to establish that a missing claim limitation is inherent, the Examiner must provide rationale or evidence making "clear that the missing descriptive matter is ***necessarily present*** in the thing described in the reference." *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999). As such, inherency may not be established by probabilities or possibilities and "[t]he mere fact that a certain thing *may* result from a given set of circumstances is not sufficient [to establish inherency]." *See In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993). "That which may be inherent is not necessarily known. Obviousness

cannot be predicated on what is unknown," even if the inherency of a certain feature is later established. *Id.*

As discussed above, none of the cited references teaches or suggests any tissue specificity of the ptxA promoter. Thus, the promoter activity in directing expression at least in leaves but not seeds as discovered by the inventors of the present application is a property of the ptxA promoter that was not known prior to the present application. The Examiner has not provided any rationale or evidence making clear that the missing descriptive matters (i.e. tissue-specific expression pattern) are *necessarily present* in the thing described in the references (i.e. the ptxA promoter). Because no rationale or evidence has been provided, a *prima facie* case of obviousness has not been established. For this additional reason, the rejection should be withdrawn.

Moreover, assuming *arguendo* the promoter activity as disclosed in the present application is an inherent property of the ptxA promoter, it has been well established that unexpected properties of a product or process can be evidence of nonobviousness in an analysis under 35 U.S.C. §103. See *In re Dillon*, 16 USPQ 2d 1897, 1901 (Fed. Cir. 1990).

Here, the specification demonstrates, through actual experimental data, the unexpected properties of the ptxA promoter. As described in Example 3 at pages 51-52 of the specification, the ptxA promoter region including the 5'-untranslated region (882 bp) was amplified from genomic DNA of pea (*Pisum sativum*) using conventional PCR method. The amplified promoter fragments of approximately 882 base pairs in length was then purified and cloned into the Bluescript plasmid, resulting the construct pBPS-ptxA (Fig. 1). Alternatively, the amplified promoter fragments were cloned directly into the vector pCR4-TOPO.

To prepare transformation vectors containing the ptxA promoter, the ptxA promoter fragment in the Topo vector (i.e. pCR4-TOPO) was isolated and cloned into upstream of a GUS reporter gene in the vector pUC. The ptxA::GUS chimeric constructs in pUC were then isolated and cloned into a binary vector for plant transformation. For monocotyledonous plant transformation, an intron of interest was amplified by PCR and cloned into the 5'-untranslated region so that the intron of interest is located between downstream of the promoter and upstream of the reporter gene. See Example 4 at page 53.

The binary vectors containing the ptxA::GUS chimeric constructs as described above were then used for *Agrobacterium*-mediated transformation with both dicotyledonous (e.g. Arabidopsis and canola) and monocotyledonous (e.g. maize) plants. Transgenic plants containing the desired construct were then regenerated. See Example 5 at pages 53-54.

By analyzing the expression pattern of the GUS reporter gene in the transgenic plants so obtained, the tissue specificity of the ptxA promoter was determined. For instance, in the transgenic Arabidopsis plants containing the ptxA::GUS chimeric constructs, the expression of the GUS reporter gene was observed, by GUS staining method, to be strong, constitutive and ubiquitous in most tissues and organs at different developmental stages, but very low level or no expression in seeds. See Example 7 at pages 55-56 and Fig. 3A-3G. As summarized in Table 1 at page 56, strong ubiquitous expression was detected in young seedlings, but only low expression was observed in the organs at the reproductive stages (e.g. siliques and flowers). Contrary to the above observations, no GUS expression was detected in seeds. A similar expression pattern was observed in the transgenic canola plants. See Table 1 at page 56 and Fig. 4A-4G.

The above observation based on GUS histochemical assays was further confirmed in T_2 and T_3 Arabidopsis lines. See Example 16 at page 61. Moreover, the GUS expression in tissues in the vegetative stages was also measured at the mRNA levels using real-time RT-PCR method. See Example 16 at pages 61-62 and Table 2. In this experiment, at least 5 different T_3 Arabidopsis lines were used (i.e. D31, D36, D52, D69, and D54, see Table 2 at page 61), and 5 independent events were tested with each T_3 Arabidopsis line (page 62, line 6). As summarized at page 61, lines 21-30, the real time RT-PCR results further indicate that the ptxA promoter controls medium to strong expression in most tissues in the vegetative stages, which supports the observation made with the GUS histochemical assays.

The expression patterns observed in transgenic Arabidopsis and canola plants as discussed above are entirely surprising and unexpected. As discussed in the specification, the promoter region of the ptxA gene from *Pisum sativum* shares approximately 50% sequence identity with the promoter region of *Medicago sativa* proline-rich protein (MsPRP2) gene. In some regions, the sequence identity is as high as 87% over 100 consecutive base pairs. Specification at page 18, lines 23-26. Since the sequence similarity between the ptxA protein

and the MsPRP2 protein is also very high (see Fig. 6a and 6b), one would expect that these two genes might belong to the same gene family. As such, one would expect that the ptxA gene would likely have a similar expression pattern as the MsPRP2 gene and so the ptxA promoter is likely having a similar promoter activity as that of the MsPRP2 promoter, particularly when these two promoter sequences share a significant degree of homology. The MsPRP2 promoter is described as being both root-specific and salt-inducible. See Specification at page 18, lines 36-37 (citing Bastola 1998 and WO 99/53016). However, as demonstrated in the present application by actual experimental data, rather than root-specific and/or salt-inducible as the MsPRP2 promoter, the ptxA promoter exhibits tissue specificity in directing expression at least in leaves but not seeds. Such an expression profile is significantly different from what one would expect based on the sequence similarity with the MsPRP2 promoter, and thus, surprising and unexpected. Because this surprising and unexpected property of the ptxA promoter is evidence of nonobviousness in an analysis under 35 U.S.C. §103, the rejection should be withdrawn for this additional reason. *See In re Dillon*, 16 USPQ 2d 1897, 1901 (Fed. Cir. 1990) (although unrecognized properties are not evidence of novelty in an anticipation analysis, the unexpected properties of a product or process are evidence of nonobviousness in an analysis under 35 U.S.C. §103).

For the above reasons and for the reasons already of record, Applicants respectfully submit that the cited references, alone or in combination, do not render the claimed subject matter obvious. Applicants additionally submit that the surprising and unexpected property of the ptxA promoter as disclosed in the present application and discussed in more detail above further evidences nonobviousness of the claimed subject matter. Accordingly, reconsideration and withdrawal of the rejections is respectfully requested.

CONCLUSION

For at least the above reasons, Applicants respectfully request withdrawal of the rejections and allowance of the claims. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

Applicants reserve all rights to pursue the non-elected subject matter in one or more divisional applications, if necessary.

The discussion above concerning the discovery of unexpected property of the ptxA promoter can be can be verified (in a declaration) if necessary.

This response is filed within the three-month period for response from the mailing of the Office Communication. No fee is believed due. However, if a fee is due, please charge our Deposit Account No. 03-2775, under Order No. 13987-00021-US from which the undersigned is authorized to draw.

Respectfully submitted,

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